

Remarks

Applicants respectfully request that the above amendments be entered prior to further examination. Claims 53, and 57-102 remain in this application, claims 1-52, and 54-56 have been canceled and new claim 103 has been added to the application.

Applicants point out that a certified translation of the priority document was submitted on April 3, 2003 and thus Pima is not available as a reference.

In addition, applicants point out that Versalovic described the identification and further analyses of two point mutations within the 23S rRNA of *Helicobacter pylori* which correlate with the resistance of some bacteria to the macrolide antibiotic Clarithromycin. Versalovic used purified genomic DNA for the identification process and the subsequent analyses, which required the isolation of the bacterium from the clinical sample and multiplication of the isolated bacterium in culture medium. Versalovic used PCR and DNA sequencing or restriction fragment analysis for the detection of point mutations. This methodology was also used by Amann for determination of a point mutation which differentiates the JG1- and LH1- subtypes of fibrobacter from each other. Amann did not succeed in clearly discriminating both subtypes by in-situ hybridization and for this reason he used state of the art methodology not in situ hybridization. Therefore, Versalovic and Amann lead away from the use of in situ hybridization as a methodology for the detection of point mutations in rRNA due to technical difficulties. In view of the prior art inability to detect a single point mutation within rRNA by in situ hybridization it was completely unexpected that one could detect clinically relevant point mutations which appear in the 23S rRNA of bacteria that are resistant against a macrolide antibiotic such as Clarithromycin.

Applicants also point out that neither Morotomi or the Strategene catalog suggest or disclose hybridization probes specific for a region of the peptidyltransferase center

from a 23S rRNA and thus the above claims would not have been obvious over the combination of these references.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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